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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/560,372	04/28/2000	Alan R. Tall	61766/JPW/GJG	3550

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EXAMINER
PARAS JR, PETER

ART UNIT	PAPER NUMBER
1632	11

DATE MAILED: 01/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/560,372	TALL, ALAN R.	
	Examiner	Art Unit	
	Peter Paras	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-49* is/are pending in the application.

4a) Of the above claim(s) *26-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26 and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 April 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-14 and 49, in Paper No. 9 is acknowledged. The traversal is on the ground(s) that the Examiner has not shown that a serious burden would be required to examine the claims, particularly the claims of Groups I and II. This is not found persuasive because it is maintained that a separate search would be required for examining the respective groups. In particular, the Invention of Group I, directed nucleic acid sequences and host cells transformed *in vitro*, may be used in materially different methods than the methods of Groups II, a method of expressing foreign DNA in a cell. For example, the nucleic acid sequences of Group I may be used in a hybridization assay *in vitro* while the method of Group II may be used to create a transgenic non-human animal. Therefore, it is maintained that these inventions are distinct due to their divergent subject matter and are thus, separately classified and searched.

The requirement is still deemed proper and is therefore made FINAL.

Please note that after a final requirement for restriction, the Applicants, in addition to making any response due on the remainder of the action, may petition the Commissioner to review the requirement. Petition may be deferred until after final action on or allowance of claims to the invention elected, but must be filed not later than appeal. A petition will not be considered if reconsideration of the requirement was not requested. (See § 1.181.).

However, please note that as per Applicants' request, two Groups will be examined which are not thought to place an undue search burden upon the Examiner. As such Groups I (claims 1-15 and 49) and II (claims 15-25) will be examined in this instant Office action.

Claims 26-48 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9.

Claim Objections

Claim 11 is objected to because of the following informalities: claim 11 depends from two different claims that are not referred to in the alternative. Appropriate correction is required.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-15, 17-25, and 49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to a nucleotide sequence comprising a human ABC1 promoter as set forth in SEQ ID NO: 1, nucleotide sequences that hybridize to the same promoter, a nucleotide sequence that is functionally equivalent to the same promoter as well as host cells comprising a recombinant expression construct that comprises the same nucleotide sequences in operable linkage with a selected coding sequence. The claims are also directed to methods of expressing foreign DNA in a host cell using a vector comprising the same nucleotide sequences.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1116.

Applicant's invention is drawn to a human ABC1 promoter having the nucleotide sequence set forth in SEQ ID NO: 1 and methods of expressing a foreign DNA in a host cell by introducing a vector comprising a foreign DNA sequence encoding a desired polypeptide in operable linkage with the nucleotide sequence set forth in SEQ ID NO: 1. The broadest claims are directed to nucleotide sequences that are functionally equivalent to the sequence set forth in SEQ ID NO: 1 and nucleotide sequences that hybridize to the sequence set forth in SEQ ID NO: 1 [**thes sequ nc s are coll ctively t rmed variants for the**

purpos of this r j ction] and methods of using such sequences to express foreign DNA in a host cell. While the specification has described the nucleotide sequence set forth in SEQ ID NO: 1 and *in vitro* methods of expressing foreign DNA in operable linkage with the nucleotide sequence of SEQ ID NO: 1 in a host cell, the specification has not described nucleotide variants of SEQ ID NO: 1 or methods of using such to express a foreign DNA in a cell. The specification fails to describe any variants of the nucleotide sequence of SEQ ID NO: 1 that can direct expression of heterologous nucleotide sequences in a host cell. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art **as of Applicants effective filing date**. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). In the instant case, variant nucleotide sequences of SEQ ID NO: 1 and methods of directing expression of foreign DNA in a host cell using the same variant sequences lack a written description. The specification fails to describe what other nucleotide sequences fall into this genus and it was unknown as of Applicants' effective filing date that any of these nucleotide sequences would have the properties of directing expression of a heterologous nucleotide sequence in a host cell. The

skilled artisan cannot envision the detailed chemical structures of all the encompassed variants of the nucleotide sequence of SEQ ID NO: 1, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolating or using. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Note: Limiting the claims only to the human ABC promoter comprising the nucleotide sequence set forth in SEQ ID NO: 1 may be sufficient to overcome this rejection.

Claims 10-13 and 15-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a host cell transformed *in vitro* with a recombinant expression construct comprising the nucleotide sequence set forth in SEQ ID NO: 1 operably linked to a foreign nucleotide sequence encoding

a polypeptide of interest and an *in vitro* method of expressing foreign DNA in a host cell using the same recombinant expression construct, does not reasonably provide enablement for a host cell transformed *in vitro* with a recombinant expression construct comprising variants of nucleotide sequence set forth in SEQ ID NO: 1 operably linked to a foreign nucleotide sequence encoding a polypeptide of interest and an *in vitro* method of expressing foreign DNA in a host cell using the same recombinant expression construct or a host cell transformed *in vivo* with any expression construct and an *in vivo* method of expressing foreign DNA in a host cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are directed are to a host cell comprising an expression construct that comprises the nucleotide sequence set forth in SEQ ID NO: 1 (or a variant of the same) operably linked to a heterologous nucleotide sequence encoding a polypeptide of interest and methods of expressing a foreign DNA in a host cell with the same expression construct.

The specification has taught the nucleotide sequence of the human ABC promoter as set forth in the nucleotide sequence of SEQ ID NO: 1. While the specification has provided guidance and teachings that would allow the skilled artisan to use the sequence of SEQ ID NO: 1 to express a heterologous nucleic acid sequence in a host cell *in vitro* the specification has failed to provide adequate teachings, guidance, or working examples that would allow the skilled artisan to transform and express a foreign DNA sequence in a host cell *in vivo*

with an expression construct comprising the nucleotide sequence of SEQ ID NO: 1 (or variants of the same) in operable linkage with a foreign DNA sequence.

The claims are directed to host cells and methods of expressing a foreign DNA sequence in a host cell. However, the claims, when taken in light of the teachings of the specification, clearly can be interpreted to read on a host cell transformed *in vivo* and methods of expressing a nucleotide sequence in a host cell *in vivo*; such claim interpretations fall into the field of gene therapy. The specification has failed to enable any host cell transformed *in vivo* with an expression construct comprising the human ABC promoter set forth in the nucleotide sequence of SEQ ID NO: 1 or a method of expressing a foreign DNA sequence under the control of the nucleotide sequence of SEQ ID NO: 1 in a host cell *in vivo*. Furthermore, the skilled artisan could not rely on the state of the art of gene therapy for teachings to transform a cell *in vivo* because the state of the art of gene therapy is unpredictable with respect to expression of a heterologous nucleotide sequence in a host cell *in vivo*. The specification has failed to provide working examples that teach targeting of cells *in vivo*, mode of administration of an expression construct, levels of expression of a foreign DNA sequence in a host cell *in vivo,* particularly the level of expression needed to provide a therapeutic effect, and the fate of the expressed heterologous protein *in vivo*. The unpredictability of the state of the art of gene therapy is reflected by the following reviews. Verma *et al.* teach that as of 1997, "there is still no single outcome that we can point to as a success story" (page 239, col. 1). The authors go on to state, "Thus far, the problem has been an inability to deliver genes

efficiently and to obtain sustained expression" (page 239, col. 3). Anderson (1998) states that "there is still no conclusive evidence that a gene-therapy protocol has been successful in the treatment of a human disease" (page 25, col 1) and concludes, "Several major deficiencies still exist including poor delivery system, both viral and no-viral, and poor gene expression after genes are delivered" (page 30). Besides the general expectation that it will require years of further research to develop effective gene therapy (Anderson, page 30), it would require extensive research to understand the fundamental biology of the system.

Note: Limiting the claims to host cells transformed *in vitro* and methods of expressing a foreign DNA sequence in a host cell *in vitro* may be sufficient to overcome this rejection.

Thus in view of the lack of guidance and direction provided by the specification for gene therapy of any disease, it would have required one of skill in the art undue experimentation to make and use the invention as claimed.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-25 and 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 8 are indefinite as written. The term "capable of " renders the claim indefinite because it is unclear if the human ABC promoter can actually

direct transcription of a heterologous coding sequence. It is suggested to remove the term "capable of" to overcome this rejection. Claims 2-24 depend from claim 1.

Claim 49 is indefinite as written. The claim recites an isolated human ABC 1 gene comprising six exons and a promoter. The specification however has described the ABC 1 gene to span a minimum of 70KB and to contain at least 49 exons. It would appear that the meaning of term gene is inconsistent between the specification and the claim. Clarification is required.

Conclusion

No claims are allowed. The claims appear to be free of the prior art of record because the prior art of record does not teach the human ABC1 promoter comprising the nucleotide sequence set forth in SEQ ID NO: 1.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is 703-308-8340. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Clark, can be reached at 703-305-4051. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703) 308-4242 and (703) 305-3014.

Inquiries of a general nature or relating to the status of the application should be directed to Kay Pinkney whose telephone number is (703) 305-3553.

Peter Paras, Jr.

Art Unit 1632

Deborah Crouch

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